Infectious Disease Epidemiology Section
Office of Public Health, Louisiana Dept of Health & Hospitals
800-256-2748 (24 hr number) – (504) 568-5005
www.oph.dhh.state.la.us

Case definitions for Diseases of Public Health Importance

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Amebiasis (*Entamoeba histolytica)*

1990 Case Definition

Clinical description

Infection of the large intestine by *Entamoeba histolytica* may result in an illness of variable severity ranging from mild, chronic diarrhea to fulminant dysentery. Infection also may be asymptomatic. Extraintestinal infection also can occur (e.g., hepatic abscess).

Laboratory criteria for diagnosis

Intestinal amebiasis

- Demonstration of cysts or trophozoites of *E. histolytica* in stool or
- Demonstration of trophozoites in tissue biopsy or ulcer scrapings by culture or histopathology

Extraintestinal amebiasis

- Demonstration of *E. histolytica* trophozoites in extraintestinal tissue

Case classification

Confirmed, intestinal amebiasis: a clinically compatible illness that is laboratory confirmed

Confirmed, extraintestinal amebiasis: a parasitologically confirmed infection of extraintestinal tissue, or among symptomatic persons (with clinical or radiographic findings consistent with extraintestinal infection), demonstration of specific antibody against *E. histolytica* as measured by indirect hemagglutination or other reliable immunodiagnostic test (e.g., enzyme-linked immunosorbent assay)

Comment

Asymptomatic intestinal carriage of *E. histolytica* should not be reported. Among asymptomatic persons, a positive serologic test does not necessarily indicate extraintestinal amebiasis.

Anthrax *(Bacillus anthracis)*

1996 Case Definition

Clinical description

An illness with acute onset characterized by several distinct clinical forms, including the following:

- Cutaneous: a skin lesion evolving during a period of 2-6 days from a papule, through a vesicular stage, to a depressed black eschar
- Inhalation: a brief prodrome resembling a viral respiratory illness, followed by development of hypoxia and dyspnea, with radiographic evidence of mediastinal widening
- Intestinal: severe abdominal distress followed by fever and signs of septicemia
- Oropharyngeal: mucosal lesion in the oral cavity or oropharynx, cervical adenopathy and edema, and fever

Laboratory criteria for diagnosis

Isolation of *Bacillus anthracis* from a clinical specimen, or

Anthrax electrophoretic immunotransblot (EITB) reaction to the protective antigen and/or lethal factor bands in one or more serum samples obtained after onset of symptoms, or

Demonstration of *B. anthracis* in a clinical specimen by immunofluorescence

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Aseptic Meningitis

1990 Case Definition

Clinical description

A syndrome characterized by acute onset of meningeal symptoms, fever, and cerebrospinal fluid pleocytosis, with bacteriologically sterile cultures. (See Encephalitis, Arboviral.)

Laboratory criteria for diagnosis

No evidence of bacterial or fungal meningitis

Case classification

Confirmed: a clinically compatible illness diagnosed by a physician as aseptic meningitis, with no laboratory evidence of bacterial or fungal meningitis

Comment

Aseptic meningitis is a syndrome of multiple etiologies, but many cases are caused by a viral agent

Bacterial Meningitis, Other

1996 Case Definition

Clinical description

Bacterial meningitis manifests most commonly with fever, headache, and a stiff neck; the disease may progress rapidly to shock and death. However, other manifestations may be observed.

Laboratory criteria for diagnosis

Isolation of a bacterial species from the cerebrospinal fluid

Case classification

Confirmed: a clinically compatible case that is either laboratory confirmed or is accompanied by a positive blood culture

Comment

Cases of bacterial meningitis caused by *Haemophilus influenzae*, *Neisseria meningitidis*, group A *Streptococcus*, and *Listeria monocytogenes* should be reported to CDC's National Notifiable Diseases Surveillance System under the disease codes specific for these organisms. Only cases of bacterial meningitis caused by organisms other than those specified should be reported as cases of "bacterial meningitis, other."

Botulism - 1996 (Clostridium botulinum)

Case Definition

Clinical description

Ingestion of botulinum toxin results in an illness of variable severity. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Laboratory criteria for diagnosis

Detection of botulinum toxin in serum, stool, or patient's food, or

Isolation of *Clostridium botulinum* from stool

Case classification

Probable: a clinically compatible case with an epidemiologic link (e.g., ingestion of a home-canned food within the previous 48 hours)

Confirmed: a clinically compatible case that is laboratory confirmed or that occurs among persons who ate the same food as persons who have laboratory-confirmed botulism

Clinical description

An illness of infants, characterized by constipation, poor feeding, and "failure to thrive" that may be followed by progressive weakness, impaired respiration, and death

Laboratory criteria for diagnosis

Detection of botulinum toxin in stool or serum, or

Isolation of *Clostridium botulinum* from stool

Case classification

Confirmed: a clinically compatible case that is laboratory-confirmed, occurring in a child aged less than 1 year

Clinical description

An illness resulting from toxin produced by *Clostridium botulinum* that has infected a wound. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Laboratory criteria for diagnosis

Detection of botulinum toxin in serum, or

Isolation of *Clostridium botulinum* from wound

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed in a patient who has no suspected exposure to contaminated food and who has a history of a fresh, contaminated wound during the 2 weeks before onset of symptoms

Clinical description

See Botulism, Foodborne.

Laboratory criteria for diagnosis

Detection of botulinum toxin in clinical specimen, or

Isolation of *Clostridium botulinum* from clinical specimen

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed in a patient aged greater than or equal to 1 year who has no history of ingestion of suspect food and has no wounds

Brucellosis *(Brucella spp.)*

1997 Case Definition

Clinical description

An illness characterized by acute or insidious onset of fever, night sweats, undue fatigue, anorexia, weight loss, headache, and arthralgia

Laboratory criteria for diagnosis

Isolation of *Brucella* spp. from a clinical specimen, or

Fourfold or greater rise in *Brucella* agglutination titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart and studied at the same laboratory, or

Demonstration by immunofluorescence of *Brucella* spp. in a clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case or that has supportive serology (i.e., *Brucella* agglutination titer of greater than or equal to 160 in one or more serum specimens obtained after onset of symptoms)

Confirmed: a clinically compatible illness that is laboratory confirmed

Campylobacter Infection *(Campylobacter spp.)*

1990 Case Definition

Clinical description

An infection that may result in diarrheal illness of variable severity

Laboratory criteria for diagnosis

Isolation of *Campylobacter* from any clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Comment

Only confirmed cases are reported to the laboratory-based surveillance system managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC.

Cholera *(Vibrio cholerae)*

1996 Case Definition

Clinical description

An illness characterized by diarrhea and/or vomiting; severity is variable.

Laboratory criteria for diagnosis

Isolation of toxigenic (i.e., cholera toxin-producing) *Vibrio cholerae* O1 or O139 from stool or vomitus, or

Serologic evidence of recent infection

Case classification

Confirmed: a clinically compatible illness that is laboratory confirmed

Comment

Illnesses caused by strains of *V. cholerae* other than toxigenic *V. cholerae* O1 or O139 should not be reported as cases of cholera. The etiologic agent of a case of cholera should be reported as either *V. cholerae* O1 or *V. cholerae* O139. Only confirmed cases should be reported to NNDSS by state health departments.

Coccidioidomycosis *(Coccidioides immitis)*

1996 Case Definition

Clinical description

Infection may be asymptomatic or may produce an acute or chronic disease. Although the disease initially resembles an influenza-like febrile illness primarily involving the bronchopulmonary system, dissemination can occur to multiple organ systems.

Clinical case definition

An illness characterized by one or more of the following:

- Influenza-like signs and symptoms (e.g., fever, chest pain, cough, myalgia, arthralgia, and headache)
- Pneumonia or other pulmonary lesion, diagnosed by chest radiograph
- Erythema nodosum or erythema multiforme rash
- Involvement of bones, joints, or skin by dissemination
- Meningitis
- Involvement of viscera and lymph nodes

Laboratory criteria for diagnosis

Cultural, histopathologic, or molecular evidence of presence of *Coccidioides immitis*, or

Positive serologic test for coccidioidal antibodies in serum or cerebrospinal fluid by:

1. Detection of coccidioidal immunoglobulin M (IgM) by immunodiffusion, enzyme immunoassay (EIA), latex agglutination, or tube precipitin, or
2. Detection of rising titer of coccidioidal immunoglobulin G (IgG) by immunodiffusion, EIA, or complement fixation, or

Coccidioidal skin-test conversion from negative to positive after onset of clinical signs and symptoms

Case classification

Confirmed: A case that meets the clinical case definition and is laboratory confirmed.

Cryptosporidiosis *(Cryptosporidium parvum)* (crypto)

1998 Case Definition

Clinical description

An illness caused by the protozoan *Cryptosporidium parvum* and characterized by diarrhea, abdominal cramps, loss of appetite, low-grade fever, nausea, and vomiting. Infected persons may be asymptomatic. The disease can be prolonged and life-threatening in severely immunocompromised persons.

Laboratory criteria for diagnosis

Laboratory-confirmed cryptosporidiosis shall be defined as the detection—in symptomatic or asymptomatic persons—of *Cryptosporidiosis*

1. oocysts in stool by microscopic examination, or
2. in intestinal fluid or small-bowel biopsy specimens, or
3. oocyst or sporozoite antigens by immunodiagnostic methods, e.g., ELISA, or
4. by PCR techniques when routinely available, or
5. demonstration of reproductive stages in tissue preparations.

Case classification

***Confirmed, symptomatic*:** a laboratory-confirmed case associated with one of the symptoms described above

***Confirmed, asymptomatic*:** a laboratory-confirmed case associated with none of the above symptoms

Cyclosporiasis *(Cyclospora cayetanensis)*

1998 Case Definition

Clinical description

An illness of variable severity caused by the protozoan *Cyclospora cayetanensis* and commonly characterized by watery diarrhea, loss of appetite, weight loss, abdominal bloating and cramping, increased flatus, nausea, fatigue, and low-grade fever. Vomiting also may be noted. Relapses and asymptomatic infections can occur.

Laboratory criteria for diagnosis

Laboratory-confirmed cyclosporiasis shall be defined as the detection—in symptomatic or asymptomatic persons—of *Cyclospora*

1. oocysts in stool by microscopic examination, or
2. in intestinal fluid or small bowel biopsy specimens, or
3. demonstration of sporulation, or
4. DNA (by polymerase chain reaction) in stool, duodenal/jejunal aspirates or small bowel biopsy specimens.

Case classification

Confirmed, symptomatic: a laboratory-confirmed case associated with one of the symptoms described above

Confirmed, asymptomatic: a laboratory-confirmed case associated with none of the above symptoms

Dengue Fever (Dengue Hemorrhagic Fever)

1996 Case Definition

Clinical description

An acute febrile illness characterized by frontal headache, retro-ocular pain, muscle and joint pain, and rash. The principal vector is the *Aedes aegypti* mosquito and transmission usually occurs in tropical or subtropical areas. Severe manifestations (e.g., dengue hemorrhagic fever and dengue shock syndrome) are rare but may be fatal.

Laboratory criteria for diagnosis

Isolation of dengue virus from serum and/or autopsy tissue samples, or

Demonstration of a fourfold or greater rise or fall in reciprocal immunoglobulin G (IgG) or immunoglobulin M (IgM) antibody titers to one or more dengue virus antigens in paired serum samples, or

Demonstration of dengue virus antigen in autopsy tissue or serum samples by immunohistochemistry or by viral nucleic acid detection

Case classification

Probable: a clinically compatible case with supportive serologic findings (a reciprocal IgG antibody titer of greater than or equal to 1280 or a positive IgM antibody test on a single acute (late)- or convalescent-phase serum specimen to one or more dengue virus antigens)

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Dengue hemorrhagic fever is defined as an acute febrile illness with minor or major bleeding phenomena, thrombocytopenia (less than or equal to 100,000/mm^3), and evidence of plasma leakage documented by hemoconcentration (hematocrit increased by greater than or equal to 20%) or other objective evidence of increased capillary permeability. The definition of dengue shock syndrome follows all of the above criteria for dengue hemorrhagic fever and also includes hypotension or narrow pulse pressure (less than or equal to 20 mm Hg).

Diphtheria *(Corynebacterium diphtheriae)*

1995 Case Definition

Clinical description

An upper respiratory tract illness characterized by sore throat, low-grade fever, and an adherent membrane of the tonsil(s), pharynx, and/or nose

Laboratory criteria for diagnosis

Isolation of *Corynebacterium diphtheriae* from a clinical specimen, or

Histopathologic diagnosis of diphtheria

Case classification

Probable: a clinically compatible case that is not laboratory confirmed and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: a clinically compatible case that is either laboratory confirmed or epidemiologically linked to a laboratory-confirmed case

Comment

Cutaneous diphtheria should not be reported. Respiratory disease caused by nontoxigenic *C. diphtheriae* should be reported as diphtheria. All diphtheria isolates, regardless of association with disease, should be sent to the Diphtheria Laboratory, National Center for Infectious Diseases, CDC.

Ehrlichiosis (HGE, HME, other or unspecified)

2000 Case Definition

Clinical description

A tick-borne illness characterized by acute onset of fever, headache, myalgia, and/or malaise. Nausea, vomiting, or rash may be present in some cases. Clinical laboratory findings may include thrombocytopenia, leukopenia, and/or elevated liver enzymes. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes of some patients.

Three categories of confirmed or probable ehrlichiosis should be reported: 1) human ehrlichiosis caused by E. chaffeensis (HME), 2) human ehrlichiosis caused by E. phagocytophila (HGE), and 3) human ehrlichiosis (other or unspecified agent), which includes cases that cannot be easily classified by available laboratory techniques, and cases caused by novel Ehrlichia species such as E. ewingii.

Laboratory criteria for diagnosis

HME:

- Demonstration of a four-fold change in antibody titer to E. chaffeensis antigen by indirect immunofluorescence assay (IFA) in paired serum samples, or
- Positive polymerase chain reaction (PCR) assay and confirmation of E. chaffeensis DNA, or
- Identification of morulae in leukocytes, and a positive IFA titer to E. chaffeensis antigen (based on cutoff titers established by the laboratory performing the assay), or
- Immunostaining of E. chaffeensis antigen in a biopsy or autopsy sample, or
- Culture of E. chaffeensis from a clinical specimen.

HGE:

- Demonstration of a four-fold change in antibody titer to E. phagocytophila antigen by IFA in paired serum samples, or
- Positive PCR assay and confirmation of E. phagocytophila DNA, or
- Identification of morulae in leukocytes, and a positive IFA titer to E. phagocytophila antigen (based on cutoff titers established by the laboratory performing the assay), or
- Immunostaining of E. phagocytophila antigen in a biopsy or autopsy sample, or
- Culture of E. phagocytophila from a clinical specimen.

Ehrlichiosis ,human, other or unspecified agent:

Demonstration of a four-fold change in antibody titer to more than one Ehrlichia species by IFA in paired serum samples, in which a dominant reactivity cannot be established, or

Identification of an Ehrlichia species other than E. chaffeensis or E. phagocytophila by PCR, immunostaining, or culture.

Case classification

Probable: a clinically compatible illness with either a single positive IFA titer (based on cutoff titers established by the laboratory performing the test) or the visualization of morulae in leukocytes.

Confirmed: a clinically compatible illness that is laboratory-confirmed.

Encephalitis or Meningitis, Arboviral (includes California serogroup, Eastern equine, St. Louis, Western equine, West Nile, Powassan)

2001 Case Definition

Clinical description

Arboviral infections may be asymptomatic or may result in illnesses of variable severity sometimes associated with central nervous system (CNS) involvement. When the CNS is affected, clinical syndromes ranging from febrile headache to aseptic meningitis to encephalitis may occur, and these are usually indistinguishable from similar syndromes caused by other viruses. Arboviral meningitis is characterized by fever, headache, stiff neck, and pleocytosis. Arboviral encephalitis is characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction (e.g., paresis or paralysis, cranial nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, and abnormal movements).

Laboratory criteria for diagnosis

Fourfold or greater change in virus-specific serum antibody titer, or

Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid, or

Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or

Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

Case classification

Probable: an encephalitis or meningitis case occurring during a period when arboviral transmission is likely, and with the following supportive serology: 1) a single or stable (less than or equal to twofold change) but elevated titer of virus-specific serum antibodies; or 2) serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.

Confirmed: an encephalitis or meningitis case that is laboratory confirmed

Comment

Because closely related arboviruses exhibit serologic cross-reactivity, positive results of serologic tests using antigens from a single arbovirus can be misleading. In some circumstances (e.g., in areas where two or more closely related arboviruses occur, or in imported arboviral disease cases), it may be epidemiologically important to attempt to pinpoint the infecting virus by conducting cross-neutralization tests using an appropriate battery of closely related viruses. This is essential, for example, in determining

that antibodies detected against St. Louis encephalitis virus are not the result of an infection with West Nile (or dengue) virus, or vice versa, in areas where both of these viruses occur.

The seasonality of arboviral transmission is variable and depends on the geographic location of exposure, the specific cycles of viral transmission, and local climatic conditions. Reporting should be etiology-specific (see below; the six encephalitides/meningitides printed in bold are nationally reportable to CDC):

St. Louis encephalitis/meningitis

West Nile encephalitis/meningitis

Powassan encephalitis/meningitis

Eastern equine encephalitis/meningitis

Western equine encephalitis/meningitis

California serogroup viral encephalitis/meningitis (includes infections with the following viruses: La Crosse, Jamestown Canyon, snowshoe hare, trivittatus, Keystone, and California encephalitis viruses)

Other viral CNS infections transmitted by mosquitos, ticks, or midges (e.g., Venezuelan equine encephalitis/meningitis and Cache Valley encephalitis/meningitis)

Enterohemorrhagic *Escherichia coli (E. coli)*

2000 Case Definition

- Enterohemorrhagic Escherichia coli O157: H7
- Enterohemorrhagic Escherichia coli shiga toxinpositive (not serogrouped)
- Enterohemorrhagic Escherichia coli shiga toxinpositive (serogroup non-O157)

Clinical description

An infection of variable severity characterized by diarrhea (often bloody) and abdominal cramps. Illness may be complicated by hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP); asymptomatic infections also may occur.

Laboratory criteria for diagnosis

Isolation of *Escherichia coli* O157:H7 from a specimen, or

Isolation of Shiga toxin-producing *E. coli* from a clinical specimen*

Case classification

Suspect: A case of postdiarrheal HUS or TTP (see HUS case definition)

Probable: A case with isolation of *E. coli* O157 from a clinical specimen, pending confirmation of H7 or Shiga toxin production, or

A clinically compatible case that is epidemiologically linked to a confirmed or probable case, or

Identification of Shiga toxin in a specimen from a clinically compatible case, or

Definitive evidence of an elevated antibody titer to a known EHEC serotype from a clinically compatible case

Confirmed: A case that meets the laboratory criteria for diagnosis.

Comment

Laboratory-confirmed isolates are reported via the Public Health Laboratory Information System (PHLIS), which is managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC. Both probable and confirmed cases are reported to the National Notifiable Diseases Surveillance System (NNDSS), but only confirmed cases are reported to PHLIS. Confirmation is based primarily on laboratory findings.

Giardiasis *(Giardia lamblia)*

1997 Case Definition

Clinical description

An illness caused by the protozoan *Giardia lamblia* and characterized by diarrhea, abdominal cramps, bloating, weight loss, or malabsorption. Infected persons may be asymptomatic.

Laboratory criteria for diagnosis

Demonstration of *G. lamblia* cysts in stool, or

Demonstration of *G. lamblia* trophozoites in stool, duodenal fluid, or small-bowel biopsy, or

Demonstration of *G. lamblia* antigen in stool by a specific immunodiagnostic test (e.g., enzyme-linked immunosorbent assay)

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Haemophilus influenzae (Invasive Disease) (*H. influenzae*)

1997 Case Definition

Clinical description

Invasive disease caused by *Haemophilus influenzae* may produce any of several clinical syndromes, including meningitis, bacteremia, epiglottitis, or pneumonia.

Laboratory criteria for diagnosis

Isolation of *H. influenzae* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Probable: a clinically compatible case with detection of *H. influenzae* type b antigen in CSF

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease.

Hansen's Disease (Leprosy) *(Mycobacterium leprae)*

1997 Case Definition

Clinical description

A chronic bacterial disease characterized by the involvement primarily of skin as well as peripheral nerves and the mucosa of the upper airway. Clinical forms of Hansen's disease represent a spectrum reflecting the cellular immune response to *Mycobacterium leprae*. The following characteristics are typical of the major forms of the disease:

- *Tuberculoid*: one or a few well-demarcated, hypopigmented, and anesthetic skin lesions, frequently with active, spreading edges and a clearing center; peripheral nerve swelling or thickening also may occur
- *Lepromatous*: a number of erythematous papules and nodules or an infiltration of the face, hands, and feet with lesions in a bilateral and symmetrical distribution that progress to thickening of the skin
- *Borderline (dimorphous)*: skin lesions characteristic of both the tuberculoid and lepromatous forms
- *Indeterminate*: early lesions, usually hypopigmented macules, without developed tuberculoid or lepromatous features

Laboratory criteria for diagnosis

Demonstration of acid-fast bacilli in skin or dermal nerve, obtained from the full-thickness skin biopsy of a lepromatous lesion

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Hantavirus Pulmonary Syndrome (HPS)

1996 Case Definition

Clinical description

Hantavirus pulmonary syndrome (HPS), commonly referred to as hantavirus disease, is a febrile illness characterized by bilateral interstitial pulmonary infiltrates and respiratory compromise usually requiring supplemental oxygen and clinically resembling acute respiratory disease syndrome (ARDS). The typical prodrome consists of fever, chills, myalgia, headache, and gastrointestinal symptoms. Typical clinical laboratory findings include hemoconcentration, left shift in the white blood cell count, neutrophilic leukocytosis, thrombocytopenia, and circulating immunoblasts.

Clinical case definition

An illness characterized by one or more of the following clinical features:

- A febrile illness (i.e., temperature greater than 101.0 F [greater than 38.3 C]) characterized by bilateral diffuse interstitial edema that may radiographically resemble ARDS, with respiratory compromise requiring supplemental oxygen, developing within 72 hours of hospitalization, and occurring in a previously healthy person
- An unexplained respiratory illness resulting in death, with an autopsy examination demonstrating noncardiogenic pulmonary edema without an identifiable cause

Laboratory criteria for diagnosis

Detection of hantavirus-specific immunoglobulin M or rising titers of hantavirus-specific immunoglobulin G, or

Detection of hantavirus-specific ribonucleic acid sequence by polymerase chain reaction in clinical specimens, or

Detection of hantavirus antigen by immunohistochemistry

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Laboratory testing should be performed or confirmed at a reference laboratory. Because the clinical illness is nonspecific and ARDS is common, a screening case definition can be used to determine which patients to test. In general, a predisposing medical condition (e.g., chronic pulmonary disease, malignancy, trauma, burn, and surgery) is a more likely cause of ARDS than HPS, and patients who have these underlying conditions and ARDS need not be tested for hantavirus.

Hemolytic Uremic Syndrome, Post-diarrheal

1996 Case Definition

Clinical description

Hemolytic uremic syndrome (HUS) is characterized by the acute onset of microangiopathic hemolytic anemia, renal injury, and low platelet count. Thrombotic thrombocytopenic purpura (TTP) also is characterized by these features but can include central nervous system (CNS) involvement and fever and may have a more gradual onset. Most cases of HUS (but few cases of TTP) occur after an acute gastrointestinal illness (usually diarrheal).

Laboratory criteria for diagnosis

The following are both present at some time during the illness:

- Anemia (acute onset) with microangiopathic changes (i.e., schistocytes, burr cells, or helmet cells) on peripheral blood smear and
- Renal injury (acute onset) evidenced by either hematuria, proteinuria, or elevated creatinine level (i.e., greater than or equal to 1.0 mg/dL in a child aged less than 13 years or greater than or equal to 1.5 mg/dL in a person aged greater than or equal to 13 years, or greater than or equal to 50% increase over baseline)

Note: A low platelet count can usually, but not always, be detected early in the illness, but it may then become normal or even high. If a platelet count obtained within 7 days after onset of the acute gastrointestinal illness is not less than 150,000/mm3, other diagnoses should be considered.

Case classification

Probable: An acute illness diagnosed as HUS or TTP that meets the laboratory criteria in a patient who does not have a clear history of acute or bloody diarrhea in preceding 3 weeks or

An acute illness diagnosed as HUS or TTP, that a) has onset within 3 weeks after onset of an acute or bloody diarrhea and b) meets the laboratory criteria except that microangiopathic changes are not confirmed

Confirmed: an acute illness diagnosed as HUS or TTP that both meets the laboratory criteria and began within 3 weeks after onset of an episode of acute or bloody diarrhea

Comment

Some investigators consider HUS and TTP to be part of a continuum of disease. Therefore, criteria for diagnosing TTP on the basis of CNS involvement and fever are not provided because cases diagnosed clinically as postdiarrheal TTP also should meet the criteria for HUS. These cases are reported as postdiarrheal HUS.

Acute Hepatitis A

2000 **Case Definition**

Clinical criteria

An acute illness with

· discrete onset of symptoms (e.g. fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting), and
· jaundice or elevated serum aminotransferase levels (ALT/AST >80)

Laboratory criteria

· IgM antibody to hepatitis A virus (anti-HAV) positive

Case Classification

Confirmed: A case that meets the clinical case definition and is laboratory confirmed or a case that meets the clinical case definition and occurs in a person who has an epidemiologic link with a person who has laboratory-confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15-50 days before the onset of symptoms).

Comment:

To date, asymptomatic individuals who are IgM anti-HAV positive have not been included as reportable cases. However, these cases do represent incident infections and it is expected that as rates of acute disease continue to decline, the case definition will be expanded to include newly infected individuals identified on the basis of laboratory results alone. When the case definition is expanded to include asymptomatic HAV infections, these cases will need to be distinguished from symptomatic cases to ensure accurate interpretation of surveillance data.

Acute Hepatitis B

2000 Case Definition

Clinical criteria

An acute illness with:

· discrete onset of symptoms (e.g. fatigue, abdominal pain, loss of appetite, intermittent nausea, vomiting), and
· jaundice or elevated serum aminotransferase levels (ALT/AST >80)

Laboratory criteria

· IgM antibody to hepatitis B core antigen (anti-HBc) positive (preferred) or
· Hepatitis B surface antigen (HBsAg) positive, if IgM anti-HBc not done
·IgM anti-HAV negative (if done)

Case classification

Suspect: A case that meets the clinical criteria, is HBsAg positive and IgM anti-HAV negative, but was not tested for IgM anti-HBc.

Confirmed: A case that meets the clinical criteria and is IgM anti-HBc positive

Comment:

To date, asymptomatic individuals who are IgM anti-HBc positive have not been included as reportable cases. However, it is expected that as rates of acute disease continue to decline, the case definition will be expanded to include newly infected individuals identified on the basis of laboratory results alone. In expanding surveillance to include asymptomatic HBV infections, these cases will need to be distinguished from symptomatic cases to ensure accurate interpretation of surveillance data.

Chronic Hepatitis B Virus Infection

2003 Case Definition

Clinical description

Persons with chronic hepatitis B virus (HBV) infection may be asymptomatic. They may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer.

Laboratory criteria for diagnosis

Hepatitis B surface antigen (HBsAg) positive, total anti-HBc positive (if done) and IgM anti-HBc negative, OR

HBsAg positive two times at least 6 months apart.

Case classification

Suspect:* a case that is HBsAg positive but has no additional confirmatory lab results.

***Confirmed*:** a case that is laboratory confirmed.

*****Louisiana case classification.

Hepatitis, Viral, Perinatal Hepatitis B Virus Infection Acquired in the United States or U.S. Territories

1995 Case Definition

Clinical case definition

Perinatal hepatitis B in the newborn may range from asymptomatic to fulminant hepatitis.

Laboratory criteria for diagnosis:

Hepatitis B surface antigen (HBsAg) positive

Case classification

HBsAg positivity in any infant aged >1-24 months who was born in the United States or in U.S. territories to an HBsAg-positive mother

Comment

Infants born to HBsAg-positive mothers should receive hepatitis B immune globulin (HBIG) and the first dose of hepatitis B vaccine within 24 hours of birth, followed by the second and third doses of vaccine at 1 and 6 months of age, respectively. Postvaccination testing for HBsAg and anti-HBs (antibody to HBsAg) is recommended from 3 to 6 months following completion of the vaccine series. If HBIG and the initial dose of vaccine are delayed for >1 month after birth, testing for HBsAg may determine if the infant is already infected.

Acute Hepatitis C

2004 **Case Definition**

Clinical criteria

An acute illness with

· discrete onset of symptoms (such as nausea, vomiting, abdominal pain and diarrhea), and
· jaundice or elevated serum aminotransferase levels

Laboratory criteria

· Serum aminotransferase levels >7 times the upper limit of normal (ALT > 350, AST >280), **and**
· IgM anti-HAV negative, **and**
· IgM anti-HBc negative, or if not done, HBsAg negative **and**
· Antibody to hepatitis C virus (anti-HCV) screening-test-positive, **and ONE of the following:**
- Recombinant immunoblot assay [RIBA] for anti-HCV positive, **or**
- Nucleic acid testing for HCV RNA positive, **or**
- Anti-HCV screening-test-positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay (e.g., ≥3.8 for the enzyme immunoassays)

Note for above: New testing platform chemiluminescence immunoassay (VITROS anti-HCV assay) *data not available yet to calculate signal to cut-off ratio.*

Case classification

Probable*: A case that meets the clinical case definition and is anti-HCV screening-test-positive (e.g. EIA), **but**

- has not been verified by an additional more specific assay or the signal to cutoff ratio is unknown **OR**
- IgM anti-HAV and IgM anti-HBV/HBsAg results are unknown.

Confirmed: A case that meets the clinical case definition and is laboratory confirmed.

*****Louisiana case classification.

Hepatitis C Virus Infection (past or present)

2003 Case Definition

Clinical description

Most hepatitis C virus (HCV) infected persons are asymptomatic. However, many have chronic liver disease, which can range from mild to severe including cirrhosis and liver cancer.

Laboratory criteria for diagnosis

Anti-HCV positive (repeat reactive) by EIA, verified by an additional more specific assay (e.g. RIBA for anti-HCV or nucleic acid testing for HCV RNA), OR

HCV RIBA positive, OR

Nucleic acid test for HCV RNA positive, OR

Anti-HCV positive (repeat reactive) by EIA with a signal to cut-off ratio >= 3.8 (as this becomes available).

Case classification

Suspect*: a case that is anti-HCV positive (repeat reactive) by EIA and does not have alanine aminotranferase (ALT or SGPT) values above the upper limit of normal (<50), and the anti-HCV EIA result has not been verified by an additional more specific assay or the signal to cutoff ratio is unknown.

Probable: a case that is anti-HCV positive (repeat reactive) by EIA and has alanine aminotranferase (ALT or SGPT) values above the upper limit of normal (>/=50), but the anti-HCV EIA result has not been verified by an additional more specific assay or the signal to cutoff ratio is unknown.

Confirmed: a case that is laboratory confirmed and that does not meet the case definition for acute hepatitis C.

***** Louisiana case classification.

Kawasaki Syndrome

1990 Case Definition

Clinical case definition

A febrile illness of greater than or equal to 5 days' duration, with at least four of the five following physical findings and no other more reasonable explanation for the observed clinical findings:

- Bilateral conjunctival injection
- Oral changes (erythema of lips or oropharynx, strawberry tongue, or fissuring of the lips)
- Peripheral extremity changes (edema, erythema, or generalized or periungual desquamation)
- Rash
- Cervical lymphadenopathy (at least one lymph node greater than or equal to 1.5 cm in diameter)

Laboratory criteria for diagnosis

None

Case classification

Confirmed: a case that meets the clinical case definition

Comment

If fever disappears after intravenous gamma globulin therapy is started, fever may be of less than 5 days' duration, and the clinical case definition may still be met.

Legionellosis *(Legionella pneumophila)*

1996 Case Definition

Clinical description

Legionellosis is associated with two clinically and epidemiologically distinct illnesses: Legionnaires disease, which is characterized by fever, myalgia, cough, pneumonia, and Pontiac fever, a milder illness without pneumonia.

Laboratory criteria for diagnosis

Isolation of *Legionella* from respiratory secretions, lung tissue, pleural fluid, or other normally sterile fluids, or

Demonstration of a fourfold or greater rise in the reciprocal immunofluorescence antibody (IFA) titer to greater than or equal to 128 against *Legionella pneumophila* serogroup 1 between paired acute- and convalescent-phase serum specimens, or

Detection of *L. pneumophila* serogroup 1 in respiratory secretions, lung tissue, or pleural fluid by direct fluorescent antibody testing, or

Demonstration of *L. pneumophila* serogroup 1 antigens in urine by radioimmunoassay or enzyme-linked immunosorbent assay

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

The previously used category of "probable case," which was based on a single IFA titer, lacks specificity for surveillance and is no longer used.

Leptospirosis *(Leptospira interrogans)*

1997 Case Definition

Clinical description

An illness characterized by fever, headache, chills, myalgia, conjunctival suffusion, and less frequently by meningitis, rash, jaundice, or renal insufficiency. Symptoms may be biphasic.

Laboratory criteria for diagnosis

Isolation of *Leptospira* from a clinical specimen, or

Fourfold or greater increase in *Leptospira* agglutination titer between acute- and convalescent-phase serum specimens obtained greater than or equal to 2 weeks apart and studied at the same laboratory, or

Demonstration of *Leptospira* in a clinical specimen by immunofluorescence

Case classification

Probable: a clinically compatible case with supportive serologic findings (i.e., a *Leptospira* agglutination titer of greater than or equal to 200 in one or more serum specimens)

Confirmed: a clinically compatible case that is laboratory confirmed

Listeriosis *(Listeria monocytogenes)*

1999 Case Definition

Clinical description

In adults, invasive disease caused by *Listeria monocytogenes* manifests most commonly as meningitis or bacteremia; infection during pregnancy may result in fetal loss through miscarriage or stillbirth, or neonatal meningitis or bacteremia. Other manifestations can also be observed.

Laboratory criteria for diagnosis

A. Isolation of *L. monocytogenes* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)
B. In the setting of miscarriage or stillbirth, isolation of *L. monocytogenes* from placental or fetal tissue

Case classification

Confirmed: A clinically compatible case that is laboratory-confirmed

Comment:

The usefulness of other laboratory methods such fluorescent antibody testing or polymerase chain reaction to diagnose invasive listeriosis has not been established.

Lyme Disease *(Borrelia burgdorferi)*

1996 Case Definition

Clinical description

A systemic, tickborne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The best clinical marker for the disease is the initial skin lesion (i.e., erythema migrans [EM]) that occurs in 60%-80% of patients.

Laboratory criteria for diagnosis

Isolation of *Borrelia burgdorferi* from a clinical specimen or

Demonstration of diagnostic immunoglobulin M or immunoglobulin G antibodies to *B. burgdorferi* in serum or cerebrospinal fluid (CSF). A two-test approach using a sensitive enzyme immunoassay or immunofluorescence antibody followed by Western blot is recommended (7).

Case classification

Confirmed: a) a case with EM or b) a case with at least one late manifestation (as defined below) that is laboratory confirmed.

Comment

This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis.

Definition of terms used in the clinical description and case definition:

- *Erythema migrans*. For purposes of surveillance, EM is defined as a skin lesion that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach greater than or equal to 5 cm in size. Secondary lesions also may occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM. For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent. The diagnosis of EM must be made by a physician. Laboratory confirmation is recommended for persons with no known exposure.
- *Late manifestations*. Late manifestations include any of the following when an alternate explanation is not found:
    1. *Musculoskeletal system*. Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints. Manifestations not considered as criteria for diagnosis include chronic progressive arthritis not preceded by brief attacks and chronic symmetrical polyarthritis. Additionally, arthralgia, myalgia, or fibromyalgia syndromes alone are not criteria for musculoskeletal involvement.

2. *Nervous system*. Any of the following, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis. Encephalomyelitis must be confirmed by demonstration of antibody production against *B. burgdorferi* in the CSF, evidenced by a higher titer of antibody in CSF than in serum. Headache, fatigue, paresthesia, or mildly stiff neck alone are not criteria for neurologic involvement.
3. *Cardiovascular system*. Acute onset of high-grade (2nd-degree or 3rd-degree) atrioventricular conduction defects that resolve in days to weeks and are sometimes associated with myocarditis. Palpitations, bradycardia, bundle branch block, or myocarditis alone are not criteria for cardiovascular involvement.

- *Exposure*. Exposure is defined as having been (less than or equal to 30 days before onset of EM) in wooded, brushy, or grassy areas (i.e., potential tick habitats) in a county in which Lyme disease is endemic. A history of tick bite is not required.
- *Disease endemic to county*. A county in which Lyme disease is endemic is one in which at least two confirmed cases have been previously acquired or in which established populations of a known tick vector are infected with *B. burgdorferi*.

Malaria *(Plasmodium spp.)*

1995 Case Definition

Clinical description

Signs and symptoms are variable; however, most patients experience fever. In addition to fever, common associated symptoms include headache, back pain, chills, sweats, myalgia, nausea, vomiting, diarrhea, and cough. Untreated *Plasmodium falciparum* infection can lead to coma, renal failure, pulmonary edema, and death. The diagnosis of malaria should be considered for any person who has these symptoms and who has traveled to an area in which malaria is endemic. Asymptomatic parasitemia can occur among persons who have been long-term residents of areas in which malaria is endemic.

Laboratory criteria for diagnosis:

Demonstration of malaria parasites in blood films

Case classification

Confirmed: an episode of microscopically confirmed malaria parasitemia in any person (symptomatic or asymptomatic) diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country.

Comment

A subsequent attack experienced by the same person but caused by a different Plasmodium species is counted as an additional case. A subsequent attack experienced by the same person and caused by the same species in the United States may indicate a relapsing infection or treatment failure caused by drug resistance.

Blood smears from questionable cases should be referred to the National Malaria Repository, CDC, for confirmation of the diagnosis.

Cases also are classified according to the following World Health Organization categories:

- *Autochthonous*:
    - *Indigenous*: malaria acquired by mosquito transmission in an area where malaria is a regular occurrence
    - *Introduced*: malaria acquired by mosquito transmission from an imported case in an area where malaria is not a regular occurrence
- *Imported*: malaria acquired outside a specific area (e.g., the United States and its territories)
- *Induced*: malaria acquired through artificial means (e.g., blood transfusion, common syringes, or malariotherapy)
- *Relapsing*: renewed manifestation (i.e., of clinical symptoms and/or parasitemia) of malarial infection that is separated from previous manifestations of the same infection by an interval greater than any interval resulting from the normal periodicity of the paroxysms
- *Cryptic*: an isolated case of malaria that cannot be epidemiologically linked to additional cases

Measles (Rubeola)

1996 Case Definition

Clinical case definition

An illness characterized by all the following:

- a generalized rash lasting greater than or equal to 3 days
- a temperature greater than or equal to 101.0°F (greater than or equal to 38.3°C)
- cough, coryza, or conjunctivitis

Laboratory criteria for diagnosis

Positive serologic test for measles immunoglobulin M antibody, or

Significant rise in measles antibody level by any standard serologic assay, or

Isolation of measles virus from a clinical specimen

Case classification

Suspect: any febrile illness accompanied by rash

Probable: a case that meets the clinical case definition, has noncontributory or no serologic or virologic testing, and is not epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed case. A laboratory-confirmed case does not need to meet the clinical case definition.

Comment

Confirmed cases should be reported to NNDSS. An *imported* case has its source outside the country or state. Rash onset occurs within 18 days after entering the jurisdiction, and illness cannot be linked to local transmission. Imported cases should be classified as:

- *International*. A case that is imported from another country
- *Out-of-State*. A case that is imported from another state in the United States. The possibility that a patient was exposed within his or her state of residence should be excluded; therefore, the patient either must have been out of state continuously for the entire period of possible exposure (at least 7-18 days before onset of rash) or have had one of the following types of exposure while out of state: a) face-to-face contact with a person who had either a probable or confirmed case or b) attendance in the same institution as a person who had a case of measles (e.g., in a school, classroom, or day care center).

An *indigenous* case is defined as a case of measles that is not imported. Cases that are linked to imported cases should be classified as indigenous if the exposure to the imported case occurred in the reporting state. Any case that cannot be proved to be imported should be classified as indigenous.

Meningococcal Disease *(Neisseria meningitidis)*

1997 Case Definition

Clinical description

Meningococcal disease manifests most commonly as meningitis and/or meningococcemia that may progress rapidly to purpura fulminans, shock, and death. However, other manifestations might be observed.

Laboratory criteria for diagnosis

Isolation of N*eisseria meningitidis* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Probable: a case with a positive antigen test in CSF or clinical purpura fulminans in the absence of a positive blood culture

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Positive antigen test results from urine or serum samples are unreliable for diagnosing meningococcal disease.

Mumps

1999 Case Definition

Clinical case definition

An illness with acute onset of unilateral or bilateral tender, self-limited swelling of the paraotid or other salivary gland, lasting greater than or equal to 2 days, and without other apparent cause

Laboratory criteria for diagnosis

Isolation of mumps virus from clinical specimen, or

Significant rise between acute- and convalescent-phase titers in serum mumps immunoglobulin G (IgG) antibody level by any standard serologic assay, or

Positive serologic test for mumps immunoglobulin M (IgM) antibody

Case classification

Probable: a case that meets the clinical case definition, has noncontributory or no serologic or virologic testing, and is not epidemiologically linked to a confirmed or probable case.

Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed or probable case. A laboratory-confirmed case does not need to meet the clinical case definition.

Pertussis *(Bordetella pertussis)* (Whooping Cough)

1997 Case Definition

Clinical case definition

Typical Disease:
A cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or post-tussive vomiting, without other apparent cause (as reported by a health professional),

Atypical Disease*:
A persistent cough illness lasting greater than 2 weeks with or without paroxysms and inspiratory whoop

Laboratory Criteria for Diagnosis

Isolation of *Bordetella pertussis* from clinical specimen

Positive polymerase chain reaction (PCR) for *B. pertussis*

Case classification

Probable: meets the clinical case definition for typical disease, is not laboratory confirmed, and is not epidemiologically linked to a laboratory-confirmed case, OR meets the clinical case definition for atypical disease and is confirmed by positive DFA

Confirmed: a case that is culture positive and in which an acute cough illness of any duration is present; or a case that meets the clinical case definition and is confirmed by positive PCR; or a case that meets the clinical case definition and is epidemiologically linked directly to a case confirmed by either culture or PCR

Comment

The clinical case definition above is appropriate for endemic or sporadic cases. In outbreak settings, a case may be defined as a cough illness lasting at least 2 weeks (as reported by a health professional). Because direct fluorescent antibody testing of nasopharyngeal secretions has been demonstrated in some studies to have low sensitivity and variable specificity (5, 6), such testing should not be relied on as a criterion for laboratory confirmation. Serologic testing for pertussis is available in some areas but is not standardized and, therefore, should not be relied on as a criterion for laboratory confirmation.

Both probable and confirmed cases should be reported nationally.

*Louisiana clinical case definition.

Plague *(Yersinia pestis)*

1996 Case Definition

Clinical description

Plague is transmitted to humans by fleas or by direct exposure to infected tissues or respiratory droplets; the disease is characterized by fever, chills, headache, malaise, prostration, and leukocytosis that manifests in one or more of the following principal clinical forms:

- Regional lymphadenitis (bubonic plague)
- Septicemia without an evident bubo (septicemic plague)
- Plague pneumonia, resulting from hematogenous spread in bubonic or septicemic cases (secondary pneumonic plague) or inhalation of infectious droplets (primary pneumonic plague)
- Pharyngitis and cervical lymphadenitis resulting from exposure to larger infectious droplets or ingestion of infected tissues (pharyngeal plague)

Laboratory criteria for diagnosis

Presumptive

- Elevated serum antibody titer(s) to *Yersinia pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination or
- Detection of F1 antigen in a clinical specimen by fluorescent assay

Confirmatory

- Isolation of *Y. pestis* from a clinical specimen or
- Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen

Case classification

Suspect: a clinically compatible case without presumptive or confirmatory laboratory results

Probable: a clinically compatible case with presumptive laboratory results

Confirmed: a clinically compatible case with confirmatory laboratory results

Poliomyelitis, Paralytic

1997 Case Definition

Clinical case definition

Acute onset of a flaccid paralysis of one or more limbs with decreased or absent tendon reflexes in the affected limbs, without other apparent cause, and without sensory or cognitive loss

Case classification

Probable: a case that meets the clinical case definition

Confirmed: a case that meets the clinical case definition and in which the patient has a neurologic deficit 60 days after onset of initial symptoms, has died, or has unknown follow-up status

Comment

All suspected cases of paralytic poliomyelitis are reviewed by a panel of expert consultants before final classification occurs. Confirmed cases are then further classified based on epidemiologic and laboratory criteria (11). Only confirmed cases are included in Table I in the *MMWR*. Suspected cases are enumerated in a footnote to the *MMWR* table.

Psittacosis *(Chlamydia psittaci)* (Ornithosis)

1996 Case Definition

Clinical description

An illness characterized by fever, chills, headache, photophobia, cough, and myalgia

Laboratory criteria for diagnosis

Isolation of *Chlamydia psittaci* from respiratory secretions, or

Fourfold or greater increase in antibody against *C. psittaci* by complement fixation or microimmunofluorescence (MIF) to a reciprocal titer of greater than or equal to 32 between paired acute- and convalescent-phase serum specimens, or

Presence of immunoglobulin M antibody against *C. psittaci* by MIF to a reciprocal titer of greater than or equal to 16

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case or that has supportive serology (e.g., *C. psittaci* titer of greater than or equal to 32 in one or more serum specimens obtained after onset of symptoms)

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

The serologic findings by CF also may occur as a result of infection with *Chlamydia pneumoniae* or *Chlamydia trachomatis*. The MIF might be more specific for infection with *C. psittaci*, but experience with and availability of this newer test are more limited.

Q Fever *(Coxiella burnetii)*

1999 Case Definition

Clinical description

Acute infection: A febrile illness usually accompanied by rigors, myalgia, malaise, and retrobulbar headache. Severe disease can include acute hepatitis, pneumonia, and meningoencephalitis. Clinical laboratory findings may include elevated liver enzyme levels and abnormal chest film findings. Asymptomatic infections may also occur.

Chronic infection: Potentially fatal endocarditis may evolve months to years after acute infection, particularly in persons with underlying valvular disease. A chronic fatigue-like syndrome has been reported in some Q fever patients.

Laboratory criteria for diagnosis

Fourfold or greater change in antibody titer to *C. burnetii* phase II or phase I antigen in paired serum specimens ideally taken 3-6 weeks apart, or,

Isolation of *C. burnetii* from a clinical specimen by culture, or

Demonstration of *C. burnetii* in a clinical specimen by detection of antigen or nucleic acid.

Case classification

Probable: a clinically compatible or epidemiologically linked case with a single supportive Immunoglobulin G (IgG) or Immunoglobulin M (IgM) titer. Cutoff titers are determined by individual laboratories. CDC tests for IgG antibodies with an indirect immunofluorescence assay (IFA), and uses a titer of 1:128 as the cutoff for significant antibody.

Confirmed: a clinically compatible or epidemiologically linked case that is laboratory confirmed.

Rabies, Animal

1997 Case Definition

Laboratory criteria for diagnosis

A positive direct fluorescent antibody test (preferably performed on central nervous system tissue)

Isolation of rabies virus (in cell culture or in a laboratory animal)

Case classification

Confirmed: a case that is laboratory confirmed

Rabies, Human

1997 Case Definition

Clinical description

Rabies is an acute encephalomyelitis that almost always progresses to coma or death within 10 days after the first symptom.

Laboratory criteria for diagnosis

Detection by direct fluorescent antibody of viral antigens in a clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck), or

Isolation (in cell culture or in a laboratory animal) of rabies virus from saliva, cerebrospinal fluid (CSF), or central nervous system tissue, or

Identification of a rabies-neutralizing antibody titer greater than or equal to 5 (complete neutralization) in the serum or CSF of an unvaccinated person.

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Laboratory confirmation by all of the above methods is strongly recommended.

Reye Syndrome

1990 Case Definition

Clinical case definition

An illness that meets all of the following criteria:

- Acute, noninflammatory encephalopathy that is documented clinically by a) an alteration in consciousness and, if available, b) a record of the CSF containing less than or equal to 8 leukocytes/cu.mm or a histologic specimen demonstrating cerebral edema without perivascular or meningeal inflammation
- Hepatopathy documented by either a) a liver biopsy or an autopsy considered to be diagnostic of Reye syndrome or b) a threefold or greater increase in the levels of the serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), or serum ammonia
- No more reasonable explanation for the cerebral and hepatic abnormalities

Case classification

Confirmed: a case that meets the clinical case definition

Rheumatic Fever

1997 Case Definition

Clinical description

An inflammatory illness that occurs as a delayed sequela of group A streptococcal infection

Major criteria: carditis, polyarthritis, chorea, subcutaneous nodules, and erythema marginatum

Minor criteria: a) previous rheumatic fever or rheumatic heart disease; b) arthralgia; c) fever; d) elevated erythrocyte sedimentation rate, positive C-reactive protein, or leukocytosis; and e) prolonged PR interval on an electrocardiogram

Laboratory criteria for diagnosis

No specific laboratory test exists for the diagnosis of rheumatic fever

Case classification

Confirmed: an illness characterized by a) two major criteria or one major and two minor criteria (as described in Clinical Description) and b) supporting evidence of preceding group A streptococcal infection (14).

Comment

Supporting evidence to confirm streptococcal infection includes increased antistreptolysin-O or other streptococcal antibodies, throat culture positive for group A streptococcus, or recent scarlet fever. The absence of supporting evidence of preceding streptococcal infection should make the diagnosis doubtful, except in Sydenham chorea or low-grade carditis when rheumatic fever is first discovered after a long latent period from the antecedent infection.

Rocky Mountain Spotted Fever (*Rickettsia rickettsii)*

1996 Case Definition

Clinical description

A tickborne febrile illness most commonly characterized by acute onset and usually accompanied by myalgia, headache, and petechial rash (on the palms and soles in two thirds of the cases)

Laboratory criteria for diagnosis

Fourfold or greater rise in antibody titer to *Rickettsia rickettsii* antigen by immunofluorescence antibody (IFA), complement fixation (CF), latex agglutination (LA), microagglutination (MA), or indirect hemagglutination antibody (IHA) test in acute- and convalescent-phase specimens ideally taken greater than or equal to 3 weeks apart, or

Positive polymerase chain reaction assay to *R. rickettsii*, or

Demonstration of positive immunofluorescence of skin lesion (biopsy) or organ tissue (autopsy), or

Isolation of *R. rickettsii* from clinical specimen

Case classification

Probable: a clinically compatible case with a single IFA serologic titer of greater than or equal to 64 or a single CF titer of greater than or equal to 16 or other supportive serology (fourfold rise in titer or a single titer greater than or equal to 320 by Proteus OX-19 or OX-2, or a single titer greater than or equal to 128 by an LA, IHA, or MA test)

Confirmed: a clinically compatible case that is laboratory confirmed

Rubella (German measles)

1996 Case Definition

Clinical case definition

An illness that has all the following characteristics:

- Acute onset of generalized maculopapular rash
- Temperature greater than 99.0 F (greater than 37.2 C), if measured
- Arthralgia/arthritis, lymphadenopathy, or conjunctivitis

Laboratory critera for diagnosis

Isolation of rubella virus, or

Significant rise between acute- and convalescent-phase titers in serum rubella immunoglobulin G antibody level by any standard serologic assay, or

Positive serologic test for rubella immunoglobulin M (IgM) antibody

Case classification

Suspect: any generalized rash illness of acute onset

Probable: a case that meets the clinical case definition, has no or noncontributory serologic or virologic testing, and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case

Comments

Serum rubella IgM test results that are false positives have been reported in persons with other viral infections (e.g., acute infection with Epstein-Barr virus [infectious mononucleosis], recent cytomegalovirus infection, and parvovirus infection) or in the presence of rheumatoid factor. Patients who have laboratory evidence of recent measles infection are excluded.

Rubella, Congenital Syndrome

1999 Case Definition

Clinical description

Presence of any defect(s) or laboratory data consistent with congenital rubella infection. Infants with congenital rubella syndrome usually present with more than one sign or symptom consistent with congenital rubella infection. However, infants may present with a single defect. Deafness is most common single defect.

Laboratory criteria for diagnosis

Isolation of rubella virus, or

Demonstration of rubella-specific immunoglobulin M (IgM) antibody, or

Infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a twofold dilution per month).

PCR positive rubella virus

Clinical case definition

An illness, usually manifesting in infancy, resulting from rubella infection *in utero* and characterized by signs or symptoms from the following categories:
a) Cataracts/congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis), hearing impairment, pigmentary retinopathy.
b) Purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease.

Case classification

Suspect: A case with some compatible clinical findings but not meeting the criteria for a probable case.

Probable: A case that is not laboratory confirmed and that has any two complications listed in paragraph "a" of the clinical case definition or one complication from paragraph "a" and one from paragraph "b", and lacks evidence of any other etiology.

Confirmed: A clinically consistent case that is laboratory confirmed.

Infection only: A case that demonstrates laboratory evidence of infection, but without any clinical symptoms or signs.

Note

In probable cases, either or both of the eye-related findings (cataracts and congenital glaucoma) count as a single complication. In cases classified as infection only, if any compatible signs or symptoms (e.g., hearing loss) are identified later, the case is reclassified as confirmed.

Salmonellosis *(Salmonella spp.)*

1997 Case Definition

Clinical description

An illness of variable severity commonly manifested by diarrhea, abdominal pain, nausea, and sometimes vomiting. Asymptomatic infections may occur, and the organism may cause extraintestinal infections.

Laboratory criteria for diagnosis

Isolation of *Salmonella* from a clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Comment

Laboratory-confirmed isolates are reported to CDC via the Public Health Laboratory Information System (PHLIS), which is managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC. Both probable and confirmed cases are reported to the National Notifiable Diseases Surveillance System, but only confirmed cases are reported to PHLIS. Both asymptomatic infections and infections at sites other than the gastrointestinal tract, if laboratory confirmed, are considered confirmed cases that should be reported to PHLIS.

Shigellosis *(Shigella spp.)*

1997 Case Definition

Clinical description

An illness of variable severity characterized by diarrhea, fever, nausea, cramps, and tenesmus. Asymptomatic infections may occur.

Laboratory criteria for diagnosis

Isolation of *Shigella* from a clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case

Confirmed: a case that is laboratory confirmed

Comment

Laboratory-confirmed isolates are reported to CDC via the Public Health Laboratory Information System (PHLIS), which is managed by the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC. Both probable and confirmed cases are reported to the National Notifiable Diseases Surveillance System, but only confirmed cases are reported to PHLIS. Confirmation is based on laboratory findings, and clinical illness is not required.

Streptococcus Disease, Invasive, Group A *(Streptococcus pyogenes)*

1995 Case Definition

Clinical description

Invasive group A streptococcal infections may manifest as any of several clinical syndromes, including pneumonia, bacteremia in association with cutaneous infection (e.g., cellulitis, erysipelas, or infection of a surgical or nonsurgical wound), deep soft-tissue infection (e.g., myositis or necrotizing fasciitis), meningitis, peritonitis, osteomyelitis, septic arthritis, postpartum sepsis (i.e., puerperal fever), neonatal sepsis, and nonfocal bacteremia.

Laboratory criteria for diagnosis

Isolation of group A *Streptococcus* (*Streptococcus pyogenes*) by culture from a normally sterile site (e.g., blood or cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Confirmed: a case that is laboratory confirmed

Streptococcus pneumoniae, Drug-Resistant Invasive Disease

1996 Case Definition

Clinical description

Streptococcus pneumoniae causes many clinical syndromes, depending on the site of infection (e.g., acute otitis media, pneumonia, bacteremia, or meningitis).

Laboratory criteria for diagnosis

Isolation of *S. pneumoniae* from a normally sterile site (e.g., blood, cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid) and

"Nonsusceptible" isolate (i.e., intermediate- or high-level resistance of the *S. pneumoniae* isolate to at least one antimicrobial agent currently approved for use in treating pneumococcal infection (12,13)*

Case classification

Probable: a clinically compatible case caused by laboratory-confirmed culture of *S. pneumoniae* identified as "nonsusceptible" (i.e., an oxacillin zone size of less than 20 mm) when oxacillin screening is the only method of antimicrobial susceptibility testing performed

Confirmed: a clinically compatible case that is laboratory confirmed

*Resistance defined by National Committee for Clinical Laboratory Standards (NCCLS)-approved methods and NCCLS-approved interpretive minimum inhibitory concentration (MIC) standards (µg/mL) for *S. pneumoniae*. NCCLS recommends that all invasive *S. pneumoniae* isolates found to be "possibly resistant" to beta-lactams (i.e., an oxacillin zone size of less than 20 mm) by oxacillin screening should undergo further susceptibility testing by using a quantitative MIC method acceptable for penicillin, extended-spectrum cephalosporins, and other drugs as clinically indicated (11,12).

Streptococcus pneumoniae, Invasive, (Children <5 years)

2000 Case Definition

Clinical description

Streptococcus pneumoniae causes many clinical syndromes, depending on the site of infection (e.g., acute otitis media, pneumonia, bacteremia, or meningitis). Starting in 2000, a conjugate pneumococcal vaccine is recommended for prevention of pneumococcal disease in the pediatric population.

Laboratory criteria for diagnosis

Isolation of S. pneumoniae from a normally sterile site (e.g., blood, cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid)

Case classification

Confirmed: a clinically compatible case in a child less than 5 years of age caused by laboratory-confirmed culture of S. pneumoniae from a normally sterile site

Streptococcal Toxic-Shock Syndrome (STSS)

1996 Case Definition

Clinical description

Streptococcal toxic-shock syndrome (STSS) is a severe illness associated with invasive or noninvasive group A streptococcal (*Streptococcus pyogenes*) infection. STSS may occur with infection at any site but most often occurs in association with infection of a cutaneous lesion. Signs of toxicity and a rapidly progressive clinical course are characteristic, and the case-fatality rate may exceed 50%.

Clinical case definition

An illness with the following clinical manifestations occurring within the first 48 hours of hospitalization or, for a nosocomial case, within the first 48 hours of illness:

- Hypotension defined by a systolic blood pressure less than or equal to 90 mm Hg for adults or less than the fifth percentile by age for children aged less than 16 years.
- Multi-organ involvement characterized by two or more of the following:
    1. *Renal impairment*: Creatinine greater than or equal to 2 mg/dL (greater than or equal to 177 µmol/L) for adults or greater than or equal to twice the upper limit of normal for age. In patients with preexisting renal disease, a greater than twofold elevation over the baseline level.
    2. *Coagulopathy*: Platelets less than or equal to 100,000/mm^3 (less than or equal to 100 x 10^6/L) or disseminated intravascular coagulation, defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products.
    3. *Liver involvement*: Alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels greater than or equal to twice the upper limit of normal for the patient's age. In patients with preexisting liver disease, a greater than twofold increase over the baseline level.
    4. *Acute respiratory distress syndrome*: defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure or by evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia.
    5. A generalized erythematous macular rash that may desquamate.
    6. Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene.

Laboratory criteria for diagnosis

Isolation of group *A Streptococcus*.

Case classification

Probable: a case that meets the clinical case definition in the absence of another identified etiology for the illness and with isolation of group A *Streptococcus* from a nonsterile site.

Confirmed: a case that meets the clinical case definition and with isolation of group A *Streptococcus* from a normally sterile site (e.g., blood or cerebrospinal fluid or, less commonly, joint, pleural, or pericardial fluid).

Tetanus *(Clostridium tetani)*

1996 Case Definition

Clinical case definition

Acute onset of hypertonia and/or painful muscular contractions (usually of the muscles of the jaw and neck) and generalized muscle spasms without other apparent medical cause

Case classification

Confirmed: a clinically compatible case, as reported by a health-care professional

Toxic-Shock Syndrome (TSS)

1997 Case Definition

Clinical case definition

An illness with the following clinical manifestations:

- *Fever*: temperature greater than or equal to 102.0°F (greater than or equal to 38.9°C)
- *Rash*: diffuse macular erythroderma
- *Desquamation*: 1-2 weeks after onset of illness, particularly on the palms and soles
- *Hypotension*: systolic blood pressure less than or equal to 90 mm Hg for adults or less than fifth percentile by age for children aged less than16 years; orthostatic drop in diastolic blood pressure greater than or equal to 15 mm Hg from lying to sitting, orthostatic syncope, or orthostatic dizziness
- *Multisystem involvement* (three or more of the following):
    - *Gastrointestinal*: vomiting or diarrhea at onset of illness
    - *Muscular*: severe myalgia or creatine phosphokinase level at least twice the upper limit of normal
    - *Mucous membrane*: vaginal, oropharyngeal, or conjunctival hyperemia
    - *Renal*: blood urea nitrogen or creatinine at least twice the upper limit of normal for laboratory or urinary sediment with pyuria (greater than or equal to 5 leukocytes per high-power field) in the absence of urinary tract infection
    - *Hepatic*: total bilirubin, alanine aminotransferase enzyme, or asparate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory
    - *Hematologic*: platelets less than 100,000/mm^3
    - *Central nervous system*: disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent

Laboratory criteria

Negative results on the following tests, if obtained:

- Blood, throat, or cerebrospinal fluid cultures (blood culture may be positive for *Staphylococcus aureus*)
- Rise in titer to Rocky Mountain spotted fever, leptospirosis, or measles

Case classification

Probable: a case which meets the laboratory criteria and in which four of the five clinical findings described above are present

Confirmed: a case which meets the laboratory criteria and in which all five of the clinical findings described above are present, including desquamation, unless the patient dies before desquamation occurs

Trichinosis *(Trichinella spp.)* (Trichinellosis)

1996 Case Definition

Clinical description

A disease caused by ingestion of *Trichinella* larvae. The disease has variable clinical manifestations. Common signs and symptoms among symptomatic persons include eosinophilia, fever, myalgia, and periorbital edema.

Laboratory criteria for diagnosis

Demonstration of *Trichinella* larvae in tissue obtained by muscle biopsy, or

Positive serologic test for *Trichinella*

Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

In an outbreak setting, at least one case must be laboratory confirmed. Associated cases should be reported as confirmed if the patient shared an epidemiologically implicated meal or ate an epidemiologically implicated meat product and has either a positive serologic test for trichinosis or a clinically compatible illness.

Tularemia *(Francisella tularensis)*

1999 Case Definition

Clinical description

An illness characterized by several distinct forms, including the following:

- Ulceroglandular: cutaneous ulcer with regional lymphadenopathy
- Glandular: regional lymphadenopathy with no ulcer
- Oculoglandular: conjunctivitis with preauricular lymphadenopathy
- Oropharyngeal: stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy
- Intestinal: intestinal pain, vomiting, and diarrhea
- Pneumonic: primary pleuropulmonary disease
- Typhoidal: febrile illness without early localizing signs and symptoms

Clinical diagnosis is supported by evidence or history of a tick or deerfly bite, exposure to tissues of a mammalian host of *Francisella tularensis*, or exposure to potentially contaminated water.

Laboratory criteria for diagnosis

Presumptive

- Elevated serum antibody titer(s) to *F. tularensis* antigen (without documented fourfold or greater change) in a patient with no history of tularemia vaccination or
- Detection of *F. tularensis* in a clinical specimen by fluorescent assay

Confirmatory

- Isolation of *F. tularensis* in a clinical specimen or
- Fourfold or greater change in serum antibody titer to *F. tularensis* antigen

Case classification

Probable: a clinically compatible case with laboratory results indicative of presumptive infection

Confirmed: a clinically compatible case with confirmatory laboratory results

Typhoid Fever *(Salmonella typhi)*

1997 Case Definition

Clinical description

An illness caused by *Salmonella typhi* that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. However, many mild and atypical infections occur. Carriage of *S. typhi* may be prolonged.

Laboratory criteria for diagnosis

Isolation of *S. typhi* from blood, stool, or other clinical specimen

Case classification

Probable: a clinically compatible case that is epidemiologically linked to a confirmed case in an outbreak

Confirmed: a clinically compatible case that is laboratory confirmed

Comment

Isolation of the organism is required for confirmation. Serologic evidence alone is not sufficient for diagnosis. Asymptomatic carriage should not be reported as typhoid fever. Isolates of *S. typhi* are reported to the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC, through the Public Health Laboratory Information System. (See *Salmonella*.)

Varicella (Chickenpox)

1999 Case Definition

Clinical case definition

An illness with acute onset of diffuse (generalized) maculo-papulovesicular rash without other apparent cause.

Laboratory criteria for diagnosis

Isolation of varicella virus from a clinical specimen, or

Direct fluorescent antibody (DFA), or

Polymerase chain reaction (PCR), or

Significant rise in serum varicella immunoglobulin G (IgG) antibody level by any standard serologic assay

Case classification

Probable: a case that meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to another probable or confirmed case

Confirmed: a case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed or probable case

Notes

Two probable cases that are epidemiologically linked would be considered confirmed, even in the absence of laboratory confirmation.

In vaccinated persons who develop varicella more than 42 days after vaccination (breakthrough disease), the disease is almost always mild with fewer than 50 skin lesions and shorter duration of illness. The rash may also be atypical in appearance (maculopapular with few or no vesicles).

Laboratory confirmation of cases of varicella is not routinely recommended; laboratory confirmation is recommended for fatal cases and in other special circumstances.

Yellow Fever

1997 Case Definition

Clinical description

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and symptoms and, in some instances, renal failure, shock, and generalized hemorrhages

Laboratory criteria for diagnosis

Fourfold or greater rise in yellow fever antibody titer in a patient who has no history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded or

Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid

Case classification

Probable: a clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever virus [e.g., greater than or equal to 32 by complement fixation, greater than or equal to 256 by immunofluorescence assay, greater than or equal to 320 by hemagglutination inhibition, greater than or equal to 160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)

Confirmed: a clinically compatible case that is laboratory confirmed